Drug Discovery, Vol. 11, No. 27, February 1, 2016 PERSPECTIVE

ISSN 2278–540X EISSN 2278–5396

Drug Discovery

An International Journal

Ayurvedic Naturoceuticals: Evidence Based Data and Clinical Implications. Part III

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Publication History
Received: 18 December 2015
Accepted: 22 January 2016
Published: 1 February 2016

Citation
Neil K Agarwal, Shashi K Agarwal. Ayurvedic Naturoceuticals: Evidence Based Data and Clinical Implications. Part III. *Drug Discovery*, 2016, 11(27), 1-7

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1. INTRODUCTION

Ayurveda is a several millennia old Indian medical system. Data from experimental, epidemiological and clinical studies provide compelling evidence that several ayurvedic naturoceuticals not only provide prophylactic and therapeutic activity against several diseases, but may actually improve general health and promote longevity. These include herbs, oils, spices, plants, minerals and trace amounts of heavy metals. Although widely used in India, firm scientific evidence for their effectiveness has been lacking due to the small and often improperly done clinical trials. However more expansive and rigorous research is now being done, providing evidence based data on the effectiveness and safety of these natural products. In the United States, Ayurvedic medications are regulated as dietary supplements. The third part of this four part series reviews another seven popular ayurvedic supplements.

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2. DISCUSSION

This section of the four part article looks at saffron, shatavari, shilajit, triphala, turmeric, tamarind and terminalia arjuna. A review of all citations on PubMed regarding these naturoceuticals was done. We found entries as follows: saffron: 737 entries dating back to 1946; shatavari: 13 entries dating back to 1969; shilajit: 32 entries dating back to 1965; tamarind: 364 entries dating back to 1945 ; terminalis arjuna: 141 entries dating back to 1982; triphala: 84 entries dating back to 1963 and turmeric: 2554 entries dating back to 1945. Other pertinent scientific articles and studies with evidence based data were also reviewed.

2.1 Saffron

Saffron is derived from the dried stigmas of the plant Crocus sativus (Family Iridaceae). It is known as the world's most expensive spice, and is used in cooking as a seasoning and coloring agent. It is also used in pharmaceutics, cosmetics, perfumery, and textile dye-producing industries. (Gohari et al, 2013) Its rich golden yellow hue comes from a carotenoid, crocin. Its potential prophylactic and therapeutic activity against several diseases has been known for centuries. This abstract reviews evidence based prophylactic and therapeutic potential of saffron in human ailments.

2.1.1 Evidence Based Data

Traditional ayurveda ascribes anti-carcinogenic, anti-mutagenic, anti-oxidant, antidepressive and immune-modulating activities to Saffron. It may also help protect against macular degeneration and retinitis pigmentosa. Beneficial effects in depression, premenstrual syndrome and Alzheimer's disease have also been described. Saffron also has cardiovascular protective properties. (Kamalipour et al, 2011; Joukar et al, 2010) These emanate from its antioxidant, lipid lowering and anti-inflammatory properties. Saffron is a common ingredient in Mediterranean cooking, known for its cardioprotective values. Clincial studies indicate that saffron preserves hemodynamics and left ventricular function and protects platelets from aggregation and lipid peroxidation. (Jessie et al, 2005) Crocetin in saffron has antitumor activities, affecting the growth of cancer cells by inhibiting nucleic acid synthesis, enhancing anti-oxidative system, inducing apoptosis and hindering growth factor signaling pathways. (Abdullaev, 2002, Abdullaev et al, 2004; Gutheil et al, 2012) Antidepressant effects were found in some clinical studies. (Schmidt et al, 2007; Moshiri et al, 2006; Akhondzadeh et al, 2005) Ayurveda also claims that it also improves general health and promotes longevity. Saffron has more than 150 biological components in saffron stigmas, which include carotenoids like zeaxanthin, lycopene, and various α- and β-carotenes.

2.1.2 Clinical Implications

Epidemiological and clinical studies provide supportive evidence for the positive effects on certain cancers and ischemic heart disease. Further research is needed to define the possible use of saffron as a chemopreventive, cardioprotective and anti-depressant agent in clinical trials.

2.2 Shatavari

Shatavari is the tuberous root of asparagus racemosus. It is commonly found throughout Sri Lanka and India. Shatavari means "curer of a hundred diseases".

2.2.1 Evidence Based Data

Ayurvedic practitioners in India have used the shatavari root in the prevention and treatment of a host of medical ailments. (Goyal et al, 2003) Besides its use in the treatment of diarrhea and dysentery, the plant also has potent anti-dyspepsia effects. (De et al, 1997; Goel et al, 1991) Its main therapeutic interest has been in its ability to stimulate milk production during lactation, (Joglekar et al, 1967; Pandey et al. 2005, Mortel et al, 2013) due to an increase in the release of corticoids and prolactin. (Meites, 1962) Various studies have indicated immunomodulatory properties of Shatavari root extracts and formulations. (Gautam et al, 2009) In Ayurvedic literature, Asparagus racemosus has been described as a rasayana herb or an adaptogen. (Gautam et al, 2009) It has also shown some promise as a carminative, diuretic, antiseptic, nerve tonic, antimutagenic, antitumor, antifungal and immunostimulatory agent. (Edenharder 1990, Shimoyamada et al. 1990, Shao et al. 1996, Balansard & Rayband 1987) It is also thought to be an aphrodisiac (Nadkarni 1976, Chadha 1985) and may have antidiabetic properties. (Hannan et al, 2007) A. racemosus has been described as absolutely safe for long term use, and especially during pregnancy and lactation

2.2.2 Clinical Implications

Research data on the medicinal use of shatavari is insufficient to make clinical recommendations. Well-designed and well-conducted clinical trials are needed to provide evidence based data regarding the therapeutic potential of shatavari for human ailments.

2.3 Shilajit

Shilajit is a natural blackish brown powdery substance found on rocks, mainly in the Himalayas. It is formed over centuries by the gradual decomposition and microbial action on certain plants, including the Euphorbia species of cactus, molds as *Barbula, Fissidens,*

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Minium, and Thuidium and other species like *Asterella, Dumortiera, Marchantia, Pellia, Plagiochasma,* and *Stephenrencella-Anthoceros. It is also known in India as shilajatu, mimie,* or *mummiyo.*

2.3.1 Evidence Based Data

Various research studies indicate that shilajit exhibits adaptogenic, analgesic, anti-allergic, antidiabetic, anti-dyslipidemic, anti-fungal, anti-inflammatory, anti-oxidant, anti-ulcerogenic, anxiolytic and immunomodulatory properties. It has properties as a neuroprotector against cognitive decline and a memory enhancer. This may help this nutraceutical in patients with Alzhiemers disease. (Carrasco-Gallardo et al, 2012; Wilson et al, 2011; Acharya et al, 1988) It also works as a protector for high altitude stresses, stimulating the immune system and reducing tiredness, lethargy, and chronic fatigue, (Meena et al, 2010) and an enhancer of spermatogenesis. It has also been used a rejuvenator, an adaptogen - attributed to the enhanced production of ATP, (Agarwal et al, 2007) and an enhancer of the quality of life. (Mittal et al, 2009) Other traditional uses include digestive and liver disorders, epilepsy, chronic bronchitis, anemia, kidney stones, hemorrhoids, and a synergestic enhacer of other drugs. Fulvic acid acts as its main biologically active ingredient. (Ghosal et al, 1990) Its safety has been established in animal and human studies. (Stohs et al, 2013)

2.3.2 Clinical implications

Limited animal and clinical studies provide evidence for the positive modulation of congnition, protector against high altitude stresses and as a rejuvenator. However, its role as a viable nutraceutical depends on future well controlled clinical trials.

2.4 Tamarind

Tamarindus indica belongs to the family Leguminosae. It is a tropical fruit tree common in the Indian subcontinent. Its pulp is commonly used as a food ingredient in curries, chutneys, sauces, ice cream, and sherbet. The seeds, wood, bark, flowers and leaves also have significant medicinal and commercial uses. It is also used as a traditional medicine in many tropical countries. (Bhadoriya et al, 2011)

2.4.1 Evidence Based Data

Tamarindus indica L. (*Fabaceae*) exhibits antidiabetic activity, antimicrobial activity, antivenomic activity, antioxidant activity, antimalarial activity, hepatoprotective activity, antiasthmatic activity, laxative activity, and anti-hyperlipidemic activity. It is extensively used in Ayurveda for treating abdominal pain, diarrhea, helminthes infections, wound healing, cold, fever, constipation, jaundice, blood disorders, malaria, gonnorhea, eye diseases and acne. (Doughari, 2006) The plaster of leaves is applied for curing inflammation locally. (El-Siddig et al, 2006; Bhadoriya et al, 2011) It may also have antifungal properties. (Rimbau et al, 1999) Several studies have reported that T. indica fruit pulp demonstrates hypocholesterolaemic and antioxidant properties by increasing hepatic gene expression of Apo A1, Abcg5 and LDL receptor while suppressing HMG-CoA reductase and Mtp gene expressions. (Chor et al, 2013; Martinello et al, 2006) Studies also suggest a potential therapeutic value of tamarind in the treatment of diabetes mellitus. (Sole et al, 2012; Sole et al, 2013) It also has anti-inflammatory (Dighe et al, 2009) and anti-bacterial activity. (Doughari et al, 2006) The medicinal properties of T. indica have been ascribed to its compounds such as catechin, procyanidin B_2, epicatechin, tartaric acid, mucilage, pectin, arabinose, xylose, galactose, glucose, uronic acid and triterpenes. Several other biological active compounds are also present. (Bhadoriya et al, 2011)

2.4.2 Clinical Implications

Epidemiological and clinical studies provide strong evidence for the medical benefits of tamarind as an anti-diabetic, hypolipidemic and anti-bacterial. However, further work is needed to confirm the efficacy and proper dosage of the T. indica fruit pulp and other parts of the tree as a therapeutic agent.

2.5 Terminalia arjuna

Terminalia arjuna is a deciduous tree which grows all over India. Its thick, white to pinkish-gray bark has used in Ayurvedic medicine for centuries, primarily as a cardiac tonic. (Maulik et al, 2010)

2.5.1 Evidence Based Data

The cardioprotective effects of terminalia arjuna have been well studied. (Colabawalla, 1951; Vaidya, 1994) It is known to provide antidyslipidaemic, (Chander et al, 2004) hypocholesterolaemic, (Gupta et al, 2001) and antioxidant activity. (Raghavan et al, 2006) These effects have been studied and well established by various animal and human studies. (Gupta et al, 2001) Other cardiovascular effects such as antihypertensive, coronary vasodilatory and antihypertrophy effects have also been reported. (Maulik et al, 2012; Dwivedi et al, 1994; Bharani et al, 2002) It has also benefitted patients with heart failure (Bharani et al, 1995) The plant has also been found to possess antimutagenic, anticancer activity, (Kaur et al,2002) and antibacterial activity. (Singh et al, 2008) The heart-health effects of Terminalia arjuna are related to the triterpenes (arjunic acid, arjunolic acid, arjungenin, arjunglycosides), tannins, polyphenols (arjunone, arjunolone, luteolin, minerals (calcium, magnesium, zinc, and copper) and other bioactive compounds

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present in its stem bark. (Saha et al, 2012; Saha et al, 2012) It has also been used for asthma, HIVinfections, lung conditions, diarrhea, urinary problems and water retention. Other uses include bile duct disorders, scorpion stings, and poisonings. However evidence based data on these is lacking. Ingestion of terminalia arjuna appears to be safe.

2.5.2 Clinical Implications

Epidemiological and both animal and human studies provide compelling evidence based data supporting the extensive cardiovascular benefits of the bark of terminalia arjuna. Further clinical studies are needed for dose standardization, toxicity and drug interactions.

2.6 Triphala

Triphala (Sanskrit tri = three and phala = fruits), composed of equal quantities of three medicinal fruits of Terminalia chebula, Terminalia bellerica and Emblica officinalis. It is a widely used in Ayurveda as a colon cleanser, digestive, diuretic, and laxative. It is also commonly used in dentistry as an anti-bacterial agent.

2.6.1 Evidence Based Data

According to Ayurvda, triphala possesses antioxidant, antiinflammatory, antipyretic, analgesic, antimutagenic, wound healing, anticariogenic, antistress, adaptogenic, hypoglycaemic, anticancer, chemoprotective, radioprotective and chemopreventive properties. Clinical studies have also shown that Triphala works as a laxative, appetite improver and reducer of gastric hyperacidity. (Baliga et al, 2012) It has also been recognized to have antibacterial, antiviral, antifungal actions. (Srinagesh et al, 2012) Clinical studies have shown that Triphala was effective in preventing dental caries and that this effect was equal to that of chlorhexidine. (Bajaj et al, 2011; Tandon et al, 2010) It has a therapeutic potential as a chemopreventive and radioprotective agent. (Baliga, 2010; Deep et al, 2010) Its hypoglycemic activity may have a role in the treatment of diabetic patients. (Rajan et al, 2008) It may also have a promise as an anti-inflammatory agent. (Rasool et al, 2007) Animal studies suggest its use in noise and stress induced conditions. (Srikumar et al, 2006)

2.6.2 Clinical Implications

Although well revered in traditional Ayurvedic medicine, well controlled clinical studies on the therapeutic effects of triphala are lacking. Some studies do suggest a role as an antibacterial agent in mouth wash, to prevent dental caries. Widespread complementary use will depend on more robust evidence based data.

2.7 Turmeric

The rhizome of Curcuma longa, a perennial herb, is boiled, cleaned, and dried, yielding a yellow powder called turmeric. Curcumin, (diferuloylmethane) which gives the yellow color to turmeric is a major component of turmeric and is commonly used as a spice and food-coloring agent. Its essential oils are also used in perfumes. Commercially it is used as a pigment dye for textiles and religiously as a pigment for skin in ceremonial functions. Its medicinal use goes back several centuries in Ayurveda.

2.7.1 Clinical Data

Curcumin has been shown to exhibit antioxidant, anti-inflammatory, (Menon et al, 2007) antiviral, antibacterial, antifungal, antiamyloid and anticancer activities. (Zhou et al, 2011; Aggarwal et al, 2007) Its use has therefore been investigated in a wide variety of diseases. (Aggarwal et al, 2009; Aggarwal and Harikumar, 2009) It is commonly used for indigestion. Clinical studies have shown that it has an antiulcerogenic activity, including those caused by Helicobacter pylori infection, chronic ingestion of non-steroidal anti-inflammatory drugs, and exogenous substances. (Yadav et al, 2013) It also plays a therapeutic role in inflammatory bowel diseases (Baliga et al, 2012) Its anti-inflammatory actions help ameliorate arthritis (Funk et al, 2006; Jackson et al, 2006)) It also demonstrates cardioprotective effects, (Kapakos et al, 2012; Miriyala et al, 2007) including safety against adriamycin induced cardiomyopathy. (Mohamad et al, 2009) Several clinical trials are testing its therapeutic value in diseases such as multiple myeloma, pancreatic cancer, myelodysplastic syndromes, colon cancer, psoriasis and Alzheimer's disease. (Hatcher et al, 2008) Although turmeric has been used for a host of other conditions such as liver and lung diseases, depression and inflammatory and infectious skin conditions, robust clinical data remins lacking.

2.7.2 Clinical Implications

Epidemiological and clinical studies provide strong evidence for the therapeutic use of turmeric in gastrointestinal disorders and arthritis. Its cardio-protective properties also appear promising. It is relatively cheap, well tolerated and pharmacologically safe.

3. CONCLUSIONS

Ancient medicine was based on naturopathic principles, and recent well organized clinical trials are providing evidence based legitimacy to these ancient claims. This four part article evaluates twenty eight ayurvedic naturoceuticals (ayur-ceuticals) which have

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been garnering the medical interest and appreciation they deserve. However, more clinical studies need to be done, to define doses and investigate side effects, so that more targeted guidelines are made available for their clinical integration.

ACKNOWLEDGEMENT

A major part of this data was presented at the International Congress on Naturopathic Medicine, July 2014, Paris, France.

REFERENCES

1. Abdullaev FI. Cancer chemopreventive and tumoricidal properties of saffron (Crocus sativus L Exp Biol Med (Maywood). 2002 Jan;227(1):20-5.
2. Abdullaev FI, Espinosa-Aguirre JJ. Biomedical properties of saffron and its potential use in cancer therapy and chemoprevention trials. Cancer Detect Prev. 2004;28(6):426-32.
3. Acharya SB, Frotan MH, Goel RK, Tripathi SK, Das PK. Pharmacological actions of shilajit. Indian Journal of Experimental Biology. 1988;26(10):775–777.
4. Agarwal SP, Khanna R, Karmarkar R, Anwer MK, Khar RK. Shilajit: a review. Phytother Res. 2007 May;21(5):401-5.
5. Aggarwal BB, Sundaram C, Malani N, Ichikawa H. Curcumin: the Indian solid gold. Adv Exp Med Biol. 2007; 595:1-75.
6. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. Int J Biochem Cell Biol. 2009 Jan;41(1):40-59.
7. Aggarwal BB, Sung B. Pharmacological basis for the role of curcumin in chronic diseases: an age-old spice with modern targets. Trends Pharmacol Sci. 2009 Feb; 30(2):85-94
8. Akhondzadeh S, Tahmacebi-Pour N, Noorbala AA,et al. Crocus sativus L. in the treatment of mild to moderate depression: a double-blind, randomized and placebo-controlled trial. Phytother Res. 2005 Feb;19(2):148-51.
9. Bajaj N, Tandon S. The effect of Triphala and Chlorhexidine mouthwash on dental plaque, gingival inflammation, and microbial growth. Int J Ayurveda Res. 2011 Jan;2(1):29-36.
10. Balansard S & Rayband M 1987 Diuretic action of Asparagus racemosus. Critical Reviews in Society of Biology 126 954–956.
11. Baliga MS, Joseph N, Venkataranganna MV et al. Curcumin, an active component of turmeric in the prevention and treatment of ulcerative colitis: preclinical and clinical observations. Food Funct. 2012 Nov;3(11):1109-17.
12. Baliga MS. Triphala, Ayurvedic formulation for treating and preventing cancer: a review. J Altern Complement Med. 2010 Dec;16(12):1301-8.
13. Baliga MS, Meera S, Mathai B et al. Scientific validation of the ethnomedicinal properties of the Ayurvedic drug Triphala: a review. Chin J Integr Med. 2012 Dec;18(12):946-54.
14. Bhadoriya SS, Ganeshpurkar A, Narwaria J et al. Tamarindus indica: Extent of explored potential. Pharmacogn Rev. 2011 Jan;5(9):73-81.
15. Bharani A, Ganguly A, Bhargave KD. Salutary effect of Terminalia arjuna in patients with severe refractory heart failure. Int J Cardiol 1995;49:191-199.
16. Bharani A, Ganguli A, Mathur LK et a, Efficacy of Terminalia arjuna in chronic stable angina: a double-blind, placebo-controlled, crossover study comparing Terminalia arjuna with isosorbide mononitrate. Indian Heart J. 2002 Mar-Apr;54(2):170-5.
17. Carrasco-Gallardo C, Guzmán L, Maccioni RB. Shilajit: a natural phytocomplex with potential procognitive activity. Int J Alzheimers Dis. 2012;2012:674142.
18. Chadha YR 1985 The Wealth of India, vol 1, pp 468–472. New Delhi: Publication and Information Directorate.
19. Chander R, Singh K, Khanna AK et al. Antidyslipidemic and antioxidant activities of different fractions of *Terminalia arjuna* stem bark. J Clin Biochem. 2004;19:141–8.
20. Chor Yin Lim, Sarni Mat Junit, Mahmood Ameen Abdulla et al. In Vivo Biochemical and Gene Expression Analyses of the Antioxidant Activities and Hypocholesterolaemic Properties of Tamarindus indica Fruit Pulp Extract. PLoS One. 2013; 8(7): e70058.
21. Colabawalla HM. An evaluation of the cardiotonic and other properties of Terminalia arjuna. Ind Heart J. 1951;3:205–230.
22. De B, Maiti RN, Joshi VK, Agrawal VK, Goel RK. Effect of some Sitavirya drugs on gastric secretion and ulceration. Indian J Exp Biol 1997;35:1084-7.
23. Deep G, Dhiman M, Rao AR, Kale RK. Chemopreventive potential of Triphala (a composite Indian drug) on benzo(a)pyrene induced forestomach tumorigenesis in murine tumor model system. J Exp Clin Cancer Res. 2005 Dec;24(4):555-63.
24. ighe NS, Pattan1 SR, Nirmal SA, Kalkotwar RS, Gaware VM, Hole MB. Analgesic activity of Tamarindus indica. Res J Pharmacogn Phytochem. 2009;1:69–71.
25. Doughari JH. Antimicrobial Activity of Tamarindus indica Linn. Trop J Pharm Res. 2006;5:597–603.
26. Dwivedi S. Agarwal MP. Antianginal and cardioprotective effects of Terminalia arjuna, an indigenous drug, in coronary artery disease. JAPI 1994;42:287-289.
27. Edenharder R 1990 Antimutagenic activity of vegetable and fruit extracts against in vitro benzo(a)pyrene. Zeitschrift fur Gesamte Hygiene 36 144–148.
28. El-Siddig, Gunasena HP, Prasad BA, Pushpakumara DK, Ramana KV, Viyayanand P. In: *Tamarindus indica* Fruits for the Future. 1st ed. Williams JT, Smith RW, Haq N, Dunsiger Z, editors. W. Sussex, England: Southampton centre for underutilized crop RPM print and design; 2006. p.188.

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Drug Discovery, 2016, 11(27), 1-7,
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29. Funk JL, Oyarzo JN, Frye JB et al. Turmeric extracts containing curcuminoids prevent experimental rheumatoid arthritis. J Nat Prod. 2006 Mar;69(3):351-5.
30. Gautam M, Saha S, Bani S et al. Immunomodulatory activity of Asparagus racemosus on systemic Th1/Th2 immunity: implications for immunoadjuvant potential. J Ethnopharmacol. 2009 Jan 21;121(2):241-7.
31. Ghosal S. Chemistry of shilajit, an immunomodulatory Ayurvedic rasayan. Pure and Applied Chemistry. 1990;62(7):1285–1288.
32. Goel RK, Bhattacharya SK. Gastroduodenal mucosal defense and mucosal protective agents. Indian J Exp Biol 1991;29:701-14.
33. Gohari AR, Saeidnia S, Mahmoodabadi MK. An overview on saffron, phytochemicals, and medicinal properties. Pharmacogn Rev. 2013 Jan;7(13):61-6.
34. Goyal RK, Singh J, Lal H Asparagus racemosus--an update. Indian J Med Sci. 2003 Sep;57(9):408-14.
35. Gupta R, Singhal S, Goyle A et al. Antioxidant and hypocholesterolaemic effects of *Terminalia arjuna* tree-bark powder: A randomised placebo-controlled trial. J Assoc Physicians India.2001;49:231–5.
36. Gutheil WG, Reed G, Ray A, Anant S, Dhar A. Crocetin: an agent derived from saffron for prevention and therapy for cancer. Curr Pharm Biotechnol. 2012 Jan;13(1):173-9.
37. Hannan1 JMA, Lamin Marenah, Liaquat Ali. Insulin secretory actions of extracts of Asparagus racemosus root in perfused pancreas, isolated islets and clonal pancreatic β-cells. J Endocrinol January 1, 2007 192 159-168.
38. Hatcher H, Planalp R, Cho J et al. Curcumin: from ancient medicine to current clinical trials. Cell Mol Life Sci. 2008 Jun;65(11):1631-52.
39. Jackson JK, Higo T, Hunter WL, Burt HM. The antioxidants curcumin and quercetin inhibit inflammatory processes associated with arthritis. Inflamm Res. 2006;55:168–175.
40. Jessie SW, Krishnakantha TP. Inhibition of human platelet aggregation and membrane lipid peroxidation by food spice, saffron. Mol Cell Biochem. 2005 Oct;278(1-2):59-63.
41. Joglekar GV, Ahuja RH, Balwani JH. Galactogogue effect of Asparagus racemosus. Indian Med J 1967;61:165.
42. Joukar S, Najafipour H, Khaksari M, Sepehri G, Shahrokhi N, Dabiri S, Gholamhoseinian A, Hasanzadeh S. The effect of saffron consumption on biochemical and histopathological heart indices of rats with myocardial infarction. Cardiovasc Toxicol. 2010 Mar;10(1):66-71.
43. Kamalipour M and Akhondzadeh S. Cardiovascular Effects of Saffron: An Evidence-Based Review. J Tehran Heart Cent. 2011 Spring; 6(2): 59–61.
44. Kapakos G, Youreva V, Srivastava AK. Cardiovascular protection by curcumin: molecular aspects. Indian J Biochem Biophys. 2012 Oct;49(5):306-15.
45. Kaur K, Arora S, Kumar S, Nagpal A. Antimutagenic activities of acetone and methanol fractions of Terminalia arjuna. Food Chem Toxicol. 2002 Oct;40(10):1475-82.
46. Martinello F, Soares SM, Franco JJ, Santos AC, Sugohara A, et al. (2006) Hypolipemic and antioxidant activities from Tamarindus indica L. pulp fruit extract in hypercholesterolemic hamsters. Food and Chemical Toxicology 44 (6): 810–818.
47. Maulik SK, Katiyar CK. Terminalia arjuna in cardiovascular diseases: making the transition from traditional to modern medicine in India. Curr Pharm Biotechnol. 2010 Dec;11(8):855-60.
48. Maulik SK, Talwar KK. Therapeutic potential of Terminalia arjuna in cardiovascular disorders. . Am J Cardiovasc Drugs. 2012 Jun 1;12(3):157-63.
49. Meena H, Pandey HK, Arya MC, Ahmed Z. Shilajit: A panacea for high-altitude problems. Int J Ayurveda Res. 2010 Jan;1(1):37-40.
50. Meites J. Proceedings of the first international pharmacology meeting. London: Pergamon Press; 1962. Vol I. pp. 151.
51. Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. Adv Exp Med Biol. 2007;595:105-25.
52. Miriyala S, Panchatcharam M, Rengarajulu P. Cardioprotective effects of curcumin. Adv Exp Med Biol. 2007;595:359-77.
53. Mittal P, D. Kaushik, V. Gupta, P. Bansal, and S. Khokra, "Therapeutic potencial of "Shilajit Rasayana"—A Review," International Journal of Pharmaceutical and Clinical Research, vol. 1, no. 2, pp. 47–49, 2009.
54. Mohamad RH, El-Bastawesy AM, Zekry ZK, et al. The role of Curcuma longa against doxorubicin (adriamycin)-induced toxicity in rats. J Med Food. 2009 Apr;12(2):394-402.
55. Mortel M, Mehta SD. Systematic review of the efficacy of herbal galactogogues. J Hum Lact. 2013 May;29(2):154-62.
56. Moshiri E, Basti AA, Noorbala AA, Jamshidi AH, Hesameddin Abbasi S, Akhondzadeh S. Crocus sativus L. (petal) in the treatment of mild-to-moderate depression: a double-blind, randomized and placebo-controlled trial. Phytomedicine. 2006 Nov; 13(9-10):607-11.
57. Nadkarni K. Indian materia medica. 3. Bombay Popular Prakashan; Mumbai: 1998. p. 830.
58. Singh SP, Mehla RK, Singh M. Plasma hormones, metabolites, milk production, and cholesterol levels in Murrah buffaloes fed with Asparagus racemosus in transition and postpartum period. Trop Anim Health Prod. 2012 Dec;44(8):1827-32.
59. Pandey SK, Sahay A, Pandey RS, Tripathi YB. Effect of Asparagus racemosus rhizome (Shatavari) on mammary gland and genital organs of pregnant rat. Phytother Res. 2005 Aug;19(8):721-4.
60. Raghavan B, Kumari SK. Effect of *Terminalia arjuna* stem bark on antioxidant status in liver and kidney of alloxan diabetic rats. Indian J Physiol Pharmacol. 2006;50:133–42.
61. Rajan SS, Antony S. Hypoglycemic effect of triphala on selected non insulin dependent Diabetes mellitus subjects. Anc Sci Life. 2008 Jan;27(3):45-9.
62. Rasool M, Sabina EP. Antiinflammatory effect of the Indian Ayurvedic herbal formulation Triphala on adjuvant-induced arthritis in mice. Phytother Res. 2007 Sep;21(9):889-94.
63. Rimbau V, Cerdan C, Vila R Iglesias J (1999) Antiinflammatory activity of some extracts from plants used in the traditional medicine of north-African countries (II). Phytotherapy Research 13 (2): 128–132.

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64. Saha A, Pawar VM, Jayaraman S. Characterisation of Polyphenols in Terminalia arjuna Bark Extract. Indian J Pharm Sci. 2012 Jul;74(4):339-4.
65. Schmidt M, Betti G, Hensel A. Saffron in phytotherapy: pharmacology and clinical uses. Wien Med Wochenschr. 2007; 157(13-14):315-9.
66. Shao Y, Chin C-K, Ho C-T, Ma W, Garrison SA & Huang MT 1996 Anti-tumour activity of the crude saponins obtained from asparagus. Cancer Letters 104 31–36.
67. Shimoyamada M, Suzuki M, Sonta H, Maruyama M & Okubo K 1990 Antifungal activity of the saponin fraction obtained from asparagus and its active principle. Agricultural and Biological Chemistry 54 2553–2557.
68. Singh DV, Gupta MM, Santha Kumar TR et al. Antibacterial principles from the bark of *Terminalia arjuna*. Curr Sci. 2008;94:27–9.
69. Sole SS, Srinivasan BP. Aqueous extract of tamarind seeds selectively increases glucose transporter-2, glucose transporter-4, and islets' intracellular calcium levels and stimulates β-cell proliferation resulting in improved glucose homeostasis in rats with streptozotocin-induced diabetes mellitus. Nutr Res. 2012 Aug;32(8):626-36.
70. Sole SS, Srinivasan BP, Akarte AS. Anti-inflammatory action of Tamarind seeds reduces hyperglycemic excursion by repressing pancreatic β-cell damage and normalizing SREBP-1c concentration. Pharm Biol. 2013 Mar;51(3):350-60.
71. Srikumar R, Parthasarathy NJ, Manikandan S et al. Effect of Triphala on oxidative stress and on cell-mediated immune response against noise stress in rats. Mol Cell Biochem. 2006 Feb;283(1-2):67-74.
72. Srinagesh J, Krishnappa P, Somanna SN. Antibacterial efficacy of triphala against oral streptococci: an in vivo study. Indian J Dent Res. 2012 Sep-Oct;23(5):696.
73. Stohs SJ. Safety and Efficacy of Shilajit (Mumie, Moomiyo). Phytother Res. 2013 Jun 3
74. Tandon S, Gupta K, Rao S et al. Effect of Triphala mouthwash on the caries status. Int J Ayurveda Res. 2010 Apr;1(2):93-9.
75. Vaidya AB. Terminalia arjuna in cardiovascular therapy. J Assoc Physicians India. 1994 Apr;42(4):281-2.
76. Wilson E, Rajamanickam GV, Dubey GP, et al. Review on shilajit used in traditional Indian medicine. Journal of Ethnopharmacology. 2011;136(1):1–9.
77. Yadav SK, Sah AK, Jha RK et al. Turmeric (curcumin) remedies gastroprotective action. Pharmacogn Rev. 2013 Jan;7(13):42-6.
78. Zhou H, Beevers CS, Huang S.The targets of curcumin. Curr Drug Targets. 2011 Mar 1;12(3):332-47.

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